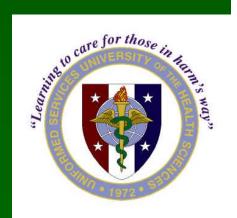
Joint USU & WRAIR Clinical Pharmacology Fellowship

Program Directors:
Louis Cantilena, MD, PhD
Colin Ohrt, MD, MPH; COL, MC

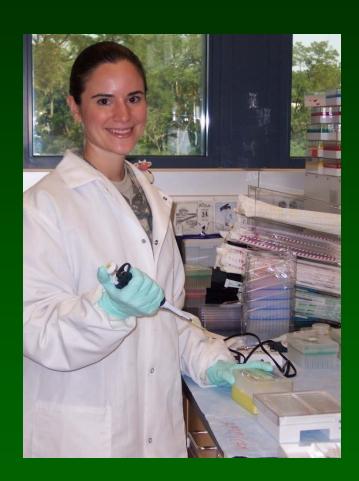






Agenda

- Fellowship
 - History
 - Curriculum
 - Institutional Support
 - Faculty
- Recent Graduates
- Fellows
- Accomplishments



CPT Lanteri – to begin fellowship July 2009

Clinical Pharmacology Fellowship

- Two-year program
- USU-WRAIR-FDA
- Fellowship Objectives
 - Train to be Clinical/Applied Pharmacologist
 - Clinical research
 - Drug development & approval
 - "Pharmacometrics"
 - Project leadership
 - "Translational medicine"
 - Board certification



MAJ Shon Remich giving 1st dose GMP artesunate overseas

Fellowship History

- Established in 1980 by Carl Peck
- AMEDD GME/LTHET Fellowship
- FDA (1989 through 1997)
- ABCP accredited since 2004
- 38 fellows graduated
- Program Directors:
 - Dr. Louis Cantilena (USU,1989)
 - COL Colin Ohrt (WRAIR, 2006)
 - Graduated from Fellowship in June 1997



Carl Peck, MD – went on to be Director CDER, FDA

Fellowship Curriculum

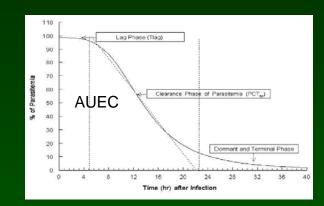
- Mentored research project
- Formal coursework
 - Principles of Clinical Pharmacology
 - Basic Pharmacology
 - Biostatics
 - Pharmacometrics
 - Ethical and Regulatory Aspects of Clinical Research
 - Introduction to the Principles and Practice of Clinical Research
 - Good Clinical Practices
- Participation in drug development teams
- Weekly Seminar/Journal Club/FDA Guidance Club
- Clinical consultations/teaching/CPU experience
- FDA rotation (3-4 months)



Educational Specialist

Fellowship Research Project

- Select in 1st six months
- Militarily relevant (US Army fellows)
- Clinical pharmacology mentor
- Areas available
 - Identification of drug candidates
 - Animal efficacy and safety testing
 - Lead optimization
 - Phase 1-2 clinical trials
 - Drug metabolism
 - Pharmacokinetics & pharmacodynamics
 - Phase IV safety monitoring
- Back-up project strongly encouraged



Institutional Support

- 3-Way MOU between WRAIR-USU-FDA
- Research projects/mentorship all
- USU lead for:
 - Medical student teaching
 - Clinical consultation
 - Clinical Pharmacology Unit
- WRAIR lead for:
 - Coordinating formal course work
 - Product development teams
 - Weekly seminars



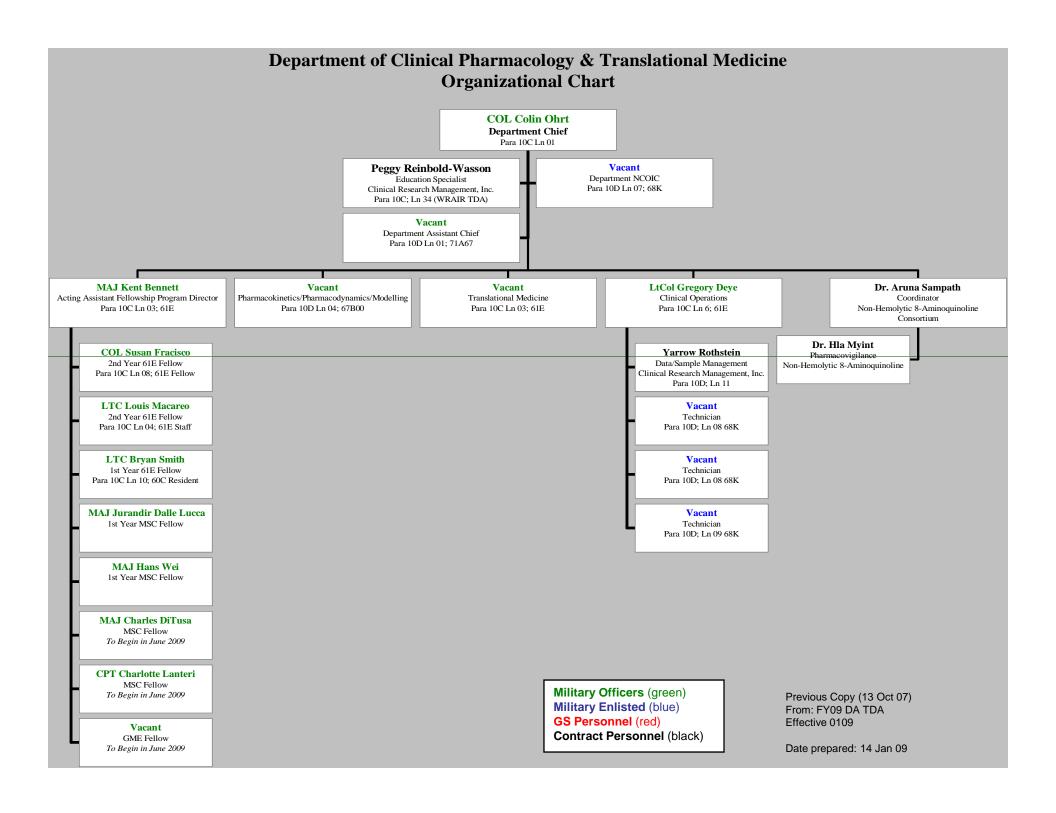
Uniformed Service University



Walter Reed Army Institute of Research

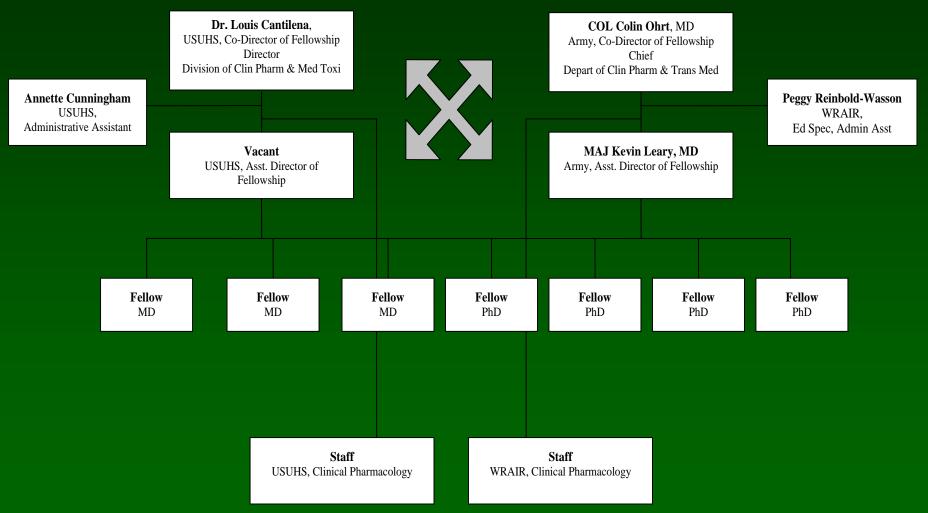
FDA – lead for: regulatory experience

Division of Experimental Therapeutic Organizational Chart Office of the Director Office of the Director Office of the Director Science Director **Deputy Director** Director (DB/0403/IV) (COL) (COL) NCOIC Admin Officer (SGT) (DJ/034/III) Secretary (DK/0318/II) Office of Director Depts Med Chem, Biology and Chemical Info Dept Clin Pharm/Trans Med **Dept Chemical Information** Dept Med Chem **Dept Parasitology** Dept Pharmacology Chief Chief Chief Chief Chief (DB/1320/III) (COL) (DB/1320/III) (DB/0403/II) (LTC) Dept Med Chem SEE ADDITIONAL Asst Chief (MAJ), 8PIs [2MAJ,4CPT, Dept Med Chem Dept Chem Info SEE ADDITIONAL Asst Chief (DB/1320/IV Dept NCOIC (SSG) & 4PIs (1MAJ/3CPT) **FLOW CHART** 1PI (DJ/0444/III) 2Civ (DB/0403/II)] **FLOW CHART** Dept NCOIC (SSG) Secretary (DK/0318/II) 7 Contractors 10 Contractors 4 Contractors **FOR BREAKDOWN** FOR BREAKDOWN 1 Tech (EM) 7 Techs(EMs) **OF DEPARTMENT** OF DEPARTMENT



Clinical Pharmacology Fellowship Organizational Chart

12 February 2009



Financial Support

- Army P8 (training)
 - ~\$105K/year
 - + Educational Specialist salary
- Army P6 (research)
 - ~\$8M/year (MIDRP)
 - External grants ~\$2-4M/year
 - Division of Experimental Therapeutics
 - Supports fellowship projects
- USU funding
 - Prior funding since 1990: NIH, FDA, US Army, and Industry \$26M
 - Currently: NCCAM (NIH) \$1.6M

Clinical Pharmacology Fellowship

- Accredited by ABCP in 2004
 - Reaccreditation in 2009
 - Internal review (2006)
 - Needs identified
 - Being implemented



Core Fellowship Faculty

Program Directors:

- Louis R. Cantilena, Jr., MD, PhD
 - Professor, Medicine and Pharmacology, USU
 - USU Clinical Pharmacology Fellowship Program Co-Director
 - Director, Division of Clinical Pharmacology and Medical Toxicology
 - ABCP Board Diplomate of Clinical Pharmacology, 1991
- Colin K. Ohrt, MD, MPH; COL, MC
 - Adjunct Associate Professor, USU
 - WRAIR Clinical Pharmacology Fellowship Program Co-Director
 - Consultant to the Surgeon General for Clinical Pharmacology
 - Chief, Department of Clinical Pharmacology and Translational Medicine
 - ABCP Board Diplomate of Clinical Pharmacology, 2003

USUHS Affiliated Core Faculty:

- Gerald H. Sokol, MD
 - Adjunct Associate Professor, Medicine
 - ABCP Board Diplomate of Clinical Pharmacology, 1991

Core Fellowship Faculty

WRAIR Affiliated Core Faculty:

- Kevin J. Leary, MD; MAJ, MC**
 - Adjunct Assistant Professor, USU
 - ABCP Board Diplomate of Clinical Pharmacology, 2007
- Kent S. Bennett, DO, PharmD, MPH; MAJ, MC**
 - Lecturer, Clinical Pharmacology and Preventive Medicine
 - Taking the ABCP Boards in 2009 if allowed to leave deployment
- R. Scott Miller, MD; COL, MC**
 - Adjunct Assistant Professor, USU
- David Saunders, MD, MPH; MAJ, MC**
 - Adjunct Assistant Professor, USU
 - Taking the ABCP Boards in 2009
- Trinka Coster, MD; COL, MC
- Kevin Cannard, MD, FAAN; (ret) COL, MC**
 - Associate Professor of Neurology and Medicine (Clinical Pharmacology), USU
 - ABCP Board Diplomate of Clinical Pharmacology, 2007

Adjunct Fellowship Faculty

USU Affiliated Adjunct Faculty:

- Daoqin Bi, MD
- Jerry M. Collins, PhD
 - ABCP Board Diplomate of Clinical Pharmacology, Charter
- Charles J. Ganley, MD
- Diane K. Jorkasky, MD
 - ABCP Board Diplomate of Clinical Pharmacology, 1992
- Daniel A. Spyker, MD, PhD
 - ABCP Board Diplomate of Clinical Pharmacology, 1991
- Curtis Wright IV, MD, MPH
 - ABCP Board Diplomate of Clinical Pharmacology, 1991

WRAIR Affiliated Adjunct Faculty:

- Ralf P. Brueckner, MD^^
- Gregory A. Deye, MD; LtCol, MC**
- Geoffrey S. Dow, PhD**
- Steven R. Gitterman, MD, PhD**
- Shiew-Mei Huang, PhD, FCP**
 - ABCP Board Diplomate of Applied Pharmacology, 2001
- Alan J. Magill, MD, FACP, FIDSA; COL, MC**
- Kirsten S. Smith, PhD; MAJ, MS**

Recent Graduates

- David Saunders, MAJ, MC
 - Graduated 2008
 - Posted at AFRIMS, Thailand
- Kent Bennett, MAJ, MC
 - Graduated 2007
 - Posted at WRAIR
- Kevin Cannard, (ret) COL, MC
 - Graduated 2006
 - Now GS civilian at WRAMC/NNMC
- Kevin Leary, MAJ, MC
 - Graduated 2005
 - Posted at USAMMDA, Ft. Detrick



MAJ David Saunders in Afghanistan before fellowship



MAJ Kevin Leary in Iraq

Fellows

- Second year
 - Susan Fracisco, COL, MC
 - Louis Macareo, LTC, MC
- First year
 - Bryan Smith, LTC, MC
 - Jurandir (JJ) DalleLucca, MAJ, MS
 - Hans Wei, MAJ, MS
- Starting in July 2009
 - Charles (Chuck) DiTusa, MAJ, MS
 - Charlotte Lanteri, CPT, MS



Clinical Pharmacology Fellowship Graduate

				CP/AP	
		Date	Date	Board	
Years	Fellow	Started	Graduated	Certified	From
80 - 81	Stambler, Nancy - MS	1-JUL-80	30-JUN-81		was a USUHS MS Student
80 - 81	Perlin, Elliot - MD	1-JUL-80	30-JUN-81	1993	was stationed USN, NNMC
81 - 83	Mell, Leroy - PhD	1-JUL-81	30-JUN-83		was stationed USN, NNRC
81 - 84	Ezra, David - MD	1-JUL-81	30-JUN-84		was from U.Tel Aviv, Israel
82 - 83	Platzer, Rudi - MD	1-JUL-82	30-JUN-83		was from U. Bern, Switzerland
82 - 84	Shmuklarsky, Mosha - MD	1-JUL-82	30-JUN-84		was from UCSF
83 - 83	Perkins, Stanley - MD	1-JAN-83	30-DEC-83		was from WRAIR
83 - 84	Chen, Benjamin - MD	1-JUL-83	30-JUN-84		was from UCSF
84 - 86	Haim, Nitin - MD	1-JUL-84	30-JUN-86		was from U.Tel Aviv, Israel
85 - 87	Hill, Vincent - MD	1-JUL-81	30-JUN-83		was from Howard U.
85 - 88	Fleischer, Nicholas - PhD	1-JUL-85	30-JUN-88		was from USUHS
86 - 87	Lehmann, Craig – PharmD	1-JUL-86	30-JUN-87		was from USAF

Clinical Pharmacology Fellowship Graduate

_				CP/AP			
		Date	Date	Board		Primary	Sub-
Years	Fellow	Started	Graduated	Certified	From	Specialty	Specialty
81 - 82	Berenberg, Jeffry - MD	1-JUL-81	30-JUN-82			Oncology	
86 - 88	Murphy, Gail - MD	1-JUL-86	30-JUN-88		Industry	Pediatrics	Neonatology
88 - 90	Brueckner, Ralf - MD	1-JUL-88	30-JUN-90		Industry	Pediatrics	
90 - 92	Ferguson, Clifford - MD	1-JUL-90	30-JUN-92		Academics	Internal Medicine	Nephrology
90 - 92	Oleshansky, Marvin - MD	1-JUL-90	30-JUN-92	1994	WRAMC	Psychiatry	
91 - 93	Marino, Mark - MD	1-JUL-91	30-JUN-93		Industry	Internal Medicine	
91 - 94	Geraci, Stephen - MD	1-JUL-91	30-JUN-94		Academics	Internal Medicine	Cardiology
91 - 94	Honig, Peter - MD	1-JUL-91	30-JUN-94		Industry		
92 - 94	Wesche, David - MD	1-JUL-92	30-JUN-94		Industry	Internal Medicine	
92 - 95	Graumlich, James - MD	1 JUL-92	30-JUN-95		Academics	Internal Medicine	
93 - 95	Hough, David - MD	1-JUL-93	30-JUN-95		Clinical Practice	Psychiatry	
93 - 96	Goldman, Steve	1-JUL-93	30-JUN-96		Industry, Consultants	Psychiatry	
94 - 96	Leo-Uhl, Kathleen - MD	1-JUL-94	30-JUN-96		FDA	Family Practice	
95 - 97	Kieffer, Lydia - PharmD	1-JUL-95	30-JUN-97		FDA		
95 - 97	Ohrt, Colin - MD						
	(Co-Director)	1-JUL-95	30-JUN-97	2003	WRAIR	Internal Medicine	
95 - 98	Pavlova, Tatiana-MD, PhD	1-JUL-95	30-JUN-98		Academics	Obstetrics-Gyn, Pediatrics	
96 - 98	Bonner, Mark - MD	1-JUL-96	30-JUN-98		Private Practice	Dermatology	
							22

**Co-Director: Dr. Louis Cantilena became a Diplomat in 1991.

Clinical Pharmacology Fellowship Graduate

				CP/AP			
		Date	Date	Board		Primary	Sub-
Years	Fellow	Started	Graduated	Certified	From	Specialty	Specialty
00 - 02	Remich, Shon - MD	1-SEP-00	31-AUG-02		WRAMC	Pediatrics	Allergy/Immun.
00 - 02	Riel, Michael - MD	1-JUL-00	30-JUN-02		Private Practice	Internal Medicine	Gastroenterology
01 - 03	Coster, Trinka - MD	1-JAN-01	31-DEC-03		OTSG	Internal Medicine	
02 - 04	Barker, Tamra - MD	1-JUL-02	30-JUN-04		Private Practice	Preventive Medicine	
02 - 04	Medlock, Matthew - MD	1-JUL-02	30-JUN-04	2005	Industry	Internal Medicine	
03 - 05	Leary, Kevin - MD	1-JUL-03	30-JUN-05	2007	USAMMDA	Internal Medicine	
04 - 06	Cannard, Kevin - MD	1-JUL-04	30-JUN-06	2007	USUHS	Neurology	Move. Disorders
05 - 07	Bennett, Kent - DO	1-JUL-05	30-JUN-07		WRAIR, ET	Preventive Medicine	
06 - 08	Saunders, David - MD	1-JUL-06	30-JUN-08		AFRIMS	Internal Medicine	
07 - 09	Fracisco, Susan - MD	1-JUL-07	30-JUN-09		WRAIR, Current MD Fellow	Psychiatry	Child Psychiatry
07 - 09	Macareo, Louis - MD	1-JUL-07	30-JUN-09		WRAIR, Current MD Fellow	Internal Medicine	
08 - 10	Smith, Bryan - MD	1-JUL-08	30-JUN-10		WRAIR, Current MD Fellow	Family Practice	
08 - 10	DalleLucca, Jurandir - PhD	1-JUL-08	30-JUN-10		WRAIR, Current PhD Fellow		
08 - 10	Wei, Hans - PhD	1-JUL-08	30-JUN-10		WRAIR, Current PhD Fellow		
09 - 11	DiTusa, Charles - PhD	1-JUL-09	30-JUN-11		WRAIR, PhD Fellow sta	rting in July '09	
09 - 11	Lanteri, Charlotte - PhD	1-JUL-09	30-JUN-11		WRAIR, PhD Fellow sta	rting in July '09	
							23

Accomplishments

- Academic Productivity
 - Abstracts: 35 by 24 fellows
 - Publications: 48 by 24 fellows*
 - 26 1st Authors
 - 6 2nd Authors
 - 4 Last Authors
 - 3 1st Author In Progress

^{*}How Journals were counted:

^{--1&}lt;sup>st</sup> Year of Fellowship: only counted journal articles in the first year of fellowship if they had published in a Clinical Pharmacology Journal

^{--2&}lt;sup>nd</sup> Year of Fellowship: Counted all of these journal articles except Commentaries

⁻⁻¹ Year following Fellowship: Counted these journal articles except Commentaries as most Fellows publish there work their 1st year out

Recent Accomplishments

- Fellows/Staff
 - Passed boards
 - MAJ Leary
 - COL Cannard
 - Awards
 - MAJ Saunders MSM for fellowship projects
 - MAJ Bennett ARCOM for fellowship projects
 - Grant Funding
 - \$1.3M MMV grant (Fracisco)
 - Mirincamycin advanced to A4 project



David Saunders, MAJ, MC

Fellowship Project

- Primary:
 - Buccal Fentayl vs IV morphine
 - Six visit cross-over design
 - Screened over 100 subjects
 - 200 study subject admissions



– Secondary:

- Doxycycline tolerability in 10th Mountain Division
- Leishmaniasis mouse model development
- IZ pharmacokinetics/team support
- Mentors: Dr. Cantilena, COL Magill
- Meritorious Service Medal for Fellow Projects/Activities

Susan Fracisco, COL, MC

Fellowship Project

- Secondary: Surrogate endpoint for malaria prevention trials
 - Led several aspects
 - Late breaker abstract ASCPT
- Primary: Mirincamycin as radical cure for malaria
 - Awarded \$450K MMV funding year one (\$1.3M total)
 - Presented historical & mouse data @ ASTMH
 - Confirmatory Rhesus study @ AFRIMS Feb 09
 - Five publications planned
 - Leading new A4 project
- Mentors: COL Ohrt, COL Magill, Dr. Carl Craft

Susan Fracisco, COL, MC

- To be posted at USU July 09
 - Medical student clin pharm teaching
 - Consultation service
 - 75% FTE WRAIR/Fellowship
 - Project leadership
 - Mirincamycin
 - Macrolide analog
 - Fellowship mentorship
 - Recruiting



Louis Macareo, LTC, MC

- Fellowship Project
 - Primary: Tinidazole for radical cure of P. vivax
 - Study recently initiated in Thailand
 - 40 days out, no relapses!
 - Secondary: PK-PD IV artesunate
 - Directly Supporting IV AS Team
 - Mentors: COL Miller, Dr. Li
- To be posted at WRAIR
 - Fellowship mentorship
 - Translational medicine
 - Clinical research
 - Overseas laboratory support
 - Recruiting
 - Mentors: COL Miller, COL Ohrt



Bryan Smith, LTC, MC

- Began 1 July 08
- Arrived from AFRIMS
- Fellowship Project
 - Primary
 - Mefloquine analogs in Aotus monkeys
 - Directly supporting Next Generation Quinoline Methanol team
 - Secondary: TBD
 - Mentors: Dr. Geoff Dow/Dr. Cantilena



Hans Wei, MAJ, MS

- Began 1 July 08
- Arrived from WRAIR
 Neurosciences
- Fellowship Project
 - Primary
 - G6PD-deficient Rhesus model
 - Directly supporting Non-hemolytic 8AQ team
 - Secondary: Antimalarial potentiation of primaquine
 - Mentors: LtCol Deye, COL Ohrt



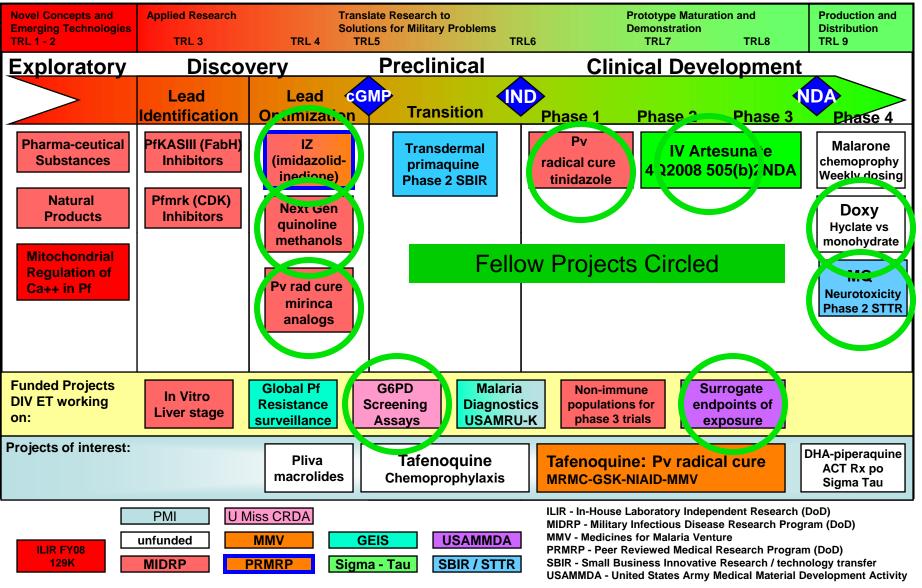
WRAIR DIV ET Anti-Malarial Drug Product Portfolio

Technology Readiness Assessment (TRL) Levels

Novel Concepts and Emerging Technologies TRL 1 - 2	Applied Research TRL 3		te Research to ns for Military Problems	rrl6	Prototype Maturation and Demonstration TRL7 TR	Distribution	
Exploratory	Disco	very	Preclinical Cli		nical Developr	ment	
	Lead Identification	Lead cGN Optimization	Transition	Phase 1	Phase 2 Pha	NDA Phase 4	
Pharma-ceutical Substances Natural Products	PfKASIII (FabH) Inhibitors Pfmrk (CDK) Inhibitors	IZ (imidazolid- inedione)	Transdermal primaquine Phase 2 SBIR	Pv radical cure tinidazole	IV Artesuna 4Q2008 505(b)2	Chemoprophy Weekly dosing Doxy	
Mitochondrial Regulation of Ca++ in Pf		quinoline methanols Pv rad cure mirinca analogs				MQ Neurotoxicity Phase 2 STTR	
Funded Projects DIV ET working on:	In Vitro Liver stage	Resistance Sc	G6PD Malar creening Diagnos Assays USAMR	stics population	ons for endpoints	of	
Projects of interest:		Pliva macrolides	Tafenoquine Chemoprophylaxis		ine: Pv radical cur (-NIAID-MMV	DHA-piperaquine ACT Rx po Sigma Tau	
ILIR FY08 129K	unfunded	MMV GE PRMRP Sigma	MIDRP - Milita MMV - Medicir PRMRP - Peer SBIR - Small E	ILIR - In-House Laboratory Independent Research (DoD) MIDRP - Military Infectious Disease Research Program (DoD) MMV - Medicines for Malaria Venture PRMRP - Peer Reviewed Medical Research Program (DoD) SBIR - Small Business Innovative Research / technology transfer USAMMDA - United States Army Medical Material Development Activity			

WRAIR DIV ET Anti-Malarial Drug Product Portfolio

Technology Readiness Assessment (TRL) Levels



Current & Recent Fellowship Resources

• P8

- Travel, courses, meetings, computers, software, library, recruiting
- Educational Specialist

• P6

- Tinidizole (\$120K)
- Mirincamycin (<\$100K)</p>
- Quinoline methanols Aotus (unused contract \$\$)

CRDA

- Mirincamycin (\$1.3M)
- Rhesus G6PD (~\$300K)

Other

- Surrogate markers (USAMMDA)
- Saunders main (USU CRDA)
- Complement inhibitor (RAD 4)

Clinical Pharmacology in Army

- Current Authorizations (11)
 - WRAIR
 - USU
 - USAMMDA (Ft. Detrick)
 - AFRIMS (Thailand)
 - USAMRU-Kenya
- Requested Authorizations
 - All MRMC laboratories
 - New Walter Reed National Military Medical Center